



General

Guideline Title

Rituximab in lymphoma and chronic lymphocytic leukemia: a clinical practice guideline, version 3.

Bibliographic Source(s)

Prisca A, Baldassarre F, Hicks LK, Imrie K, Kouroukis TC, Cheung M. Rituximab in lymphoma and chronic lymphocytic leukemia: a clinical practice guideline, version 3. Toronto (ON): Cancer Care Ontario (CCO); 2015 Mar 31. 173 p. (Evidence-based series; no. 6-8). [236 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Imrie K, Stevens A, Meyer R, Hematology Disease Site Group. Rituximab in lymphoma and chronic lymphocytic leukemia: a clinical practice guideline. Toronto (ON): Cancer Care Ontario (CCO); 2005 Dec 22. 46 p. (Evidence-based series; no. 6-8). [65 references]

The EVIDENCE-BASED SERIES report, initially the full original guideline, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the [Cancer Care Ontario Web site](#) for details on any new evidence that has emerged and implications to the guidelines.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Recommendation 1

Aggressive Histology B-cell Lymphomas, Including Burkitt Lymphoma: First-line, Second-line and Maintenance Treatment and Patients with Human Immunodeficiency Virus (HIV)-associated Lymphomas

Previously Untreated Patients

- a. Previously untreated patients with aggressive histology CD20-positive B-cell lymphomas who are candidates for treatment with curative intent and will receive combination chemotherapy with curative intent (including cyclophosphamide, doxorubicin, vincristine, and prednisone [CHOP], CHOP-like, or similar dose-intense regimens) should receive this therapy in combination with rituximab

Patients with Relapsed/Refractory Disease

- b. For previously treated patients with aggressive histology CD20-positive B-cell lymphomas:
 - i. There is insufficient evidence at this time to support treatment with a rituximab-containing chemotherapy regimen in patients who have been previously treated with a rituximab-containing chemotherapy regimen.
 - ii. If patients have not previously received rituximab as part of their treatment regimen, the addition of rituximab to chemotherapy is reasonable.

Rituximab Maintenance Treatment

- c. There is insufficient evidence at this time to support the use of maintenance rituximab in aggressive histology B-cell lymphomas.

Patients with HIV-Associated Lymphomas

- d. Previously untreated patients with HIV-related lymphoma with a CD4 count $\geq 50/\text{mm}^3$ who are candidates for treatment with curative intent and will receive combination chemotherapy with curative intent (including CHOP, CHOP-like, or similar dose-intense regimens), should receive this therapy in combination with rituximab. The addition of rituximab to chemotherapy in patients with CD4 $< 50/\text{mm}^3$ is not recommended.

Recommendation 2

Indolent Histology B-cell Lymphomas: First-line, Second-line, and Maintenance Treatment and Patients with Asymptomatic CD20-positive B-cell Lymphomas

Previously Untreated Patients

- a. Previously untreated patients with indolent histology CD20-positive B-cell lymphomas, excluding small lymphocytic lymphoma (SLL), who are appropriate candidates for chemotherapy, should receive their chemotherapy in combination with rituximab.
- b. For patients with indolent histology CD20-positive B-cell-histology lymphomas, excluding SLL, who are candidates for therapy, but not combination chemotherapy, rituximab monotherapy is a reasonable option.

Patients with Relapsed/Refractory Disease

- c. For previously treated patients with indolent histology CD20-positive B-cell lymphomas, excluding SLL:
 - i. Patients who have not previously received rituximab and who are appropriate candidates for chemotherapy should receive this chemotherapy in combination with rituximab or as rituximab monotherapy.
 - ii. Patients who have previously received rituximab (including combination rituximab chemotherapy, rituximab monotherapy, or maintenance rituximab) and who have achieved a response of at least one year's duration from the last rituximab administration and who are appropriate candidates for therapy should receive this therapy in combination with rituximab or as rituximab monotherapy.

Rituximab Maintenance Treatment

- d. For patients with indolent histology CD20-positive B-cell lymphomas, excluding SLL, who respond to treatment with combination chemotherapy and/or rituximab, this treatment should be followed by the use of maintenance rituximab.

Patients with Asymptomatic CD20-Positive B-Cell Lymphomas

- e. There is insufficient evidence at this time to support or refute upfront treatment with rituximab monotherapy for asymptomatic indolent histology CD20-positive B-cell lymphomas.

Recommendation 3

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Previously Untreated Patients

- a. Patients with previously untreated chronic lymphocytic leukemia (CLL)/SLL, who are appropriate candidates for fludarabine-based chemotherapy, should receive this treatment in combination with rituximab.
- b. In patients with previously untreated CLL/SLL who are appropriate candidates for chlorambucil chemotherapy, the addition of rituximab

can be considered.

Patients with Relapsed/Refractory Disease

- c. Patients with relapsed or refractory CLL/SLL, who are appropriate candidates for fludarabine-based chemotherapy, should receive this treatment in combination with rituximab.

Recommendation 4

Hepatitis B Virus Reactivation in All Patients Treated with Rituximab

The Hematology Disease Site Group (DSG) recommends that all patients be screened for surface antigen for hepatitis B (HBsAg) and for hepatitis B core antibody (HBcAb) prior to treatment with rituximab. Consultation with an expert in hepatitis B virus (HBV) should be considered for all patients who test positively for HBV. Patients who are HBsAg positive should receive prophylactic antiviral therapy during and after rituximab. Patients who are HBsAg negative/HBcAb positive should be considered for either prophylactic antiviral therapy, close monitoring for viral reactivation, and/or should be followed by an expert in HBV. In the absence of active hepatitis (elevated transaminases), it is not usually necessary to delay rituximab. In most cases, HBV screening and management can occur in parallel with non-Hodgkin lymphoma/CLL treatment.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Lymphoma
- Chronic lymphocytic leukemia (CLL)

Guideline Category

Assessment of Therapeutic Effectiveness

Management

Treatment

Clinical Specialty

Hematology

Oncology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To provide an updated guideline on the use of rituximab in lymphoma and chronic lymphocytic leukemia (CLL)

Target Population

- Adult patients with lymphoma of any type, at any stage, and any histology
- Adult patients with chronic lymphocytic leukemia (CLL) at any stage

Interventions and Practices Considered

1. Combination chemotherapy
2. Rituximab monotherapy
3. Maintenance rituximab for patients who respond to treatment with combination chemotherapy and/or rituximab
4. Screening for surface antigen for hepatitis B (HBsAg) and for hepatitis B core antibody (HBcAb) prior to treatment with rituximab

Note: The following interventions were considered but not recommended or there was insufficient evidence to recommend:

- Treatment with a rituximab-containing chemotherapy regimen in patients who have been previously treated with a rituximab-containing chemotherapy regimen
- Maintenance rituximab in aggressive histology B-cell lymphomas
- The addition of rituximab to chemotherapy in patients with human immunodeficiency virus (HIV)-related lymphoma with a CD4 <50/mm³
- Rituximab monotherapy for asymptomatic indolent histology CD20-positive B-cell lymphomas

Major Outcomes Considered

- Overall survival
- Disease control, as assessed by measures such as:
 - Progression-free survival
 - Event-free survival
 - Time to treatment failure
 - Response duration
- Response rate
- Quality of life
- Toxicity of rituximab alone or in combination with chemotherapy

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Strategy

For this update a search for guidelines was undertaken in the:

- Inventory of Cancer Guidelines (SAGE) (<http://www.cancerguidelines.ca/Guidelines/inventory/index.php>),
- National Guideline Clearinghouse (NGC) (<http://www.guideline.gov/>),
- Canadian Medical Association (CMA) Infobase (http://www.cma.ca/index.php/ci_id/54316/la_id/1.htm), and
- On the Web sites of international guidelines developers such as the National Institute for Health and Care Excellence (UK) (NICE), the Scottish Intercollegiate Guideline Network (SIGN), the Australian National Health and Medical Research Council, and the New Zealand Guidelines Group.

The literature was systematically searched using the electronic databases MEDLINE (Ovid, March 2006 to October 2013), EMBASE (Ovid, March 2006 to October 2013), and the Cochrane Library (Central Register of Controlled Trials, Database of Systematic Reviews and Database of Abstracts of Effects, October 22, 2013). The search strategies used for the MEDLINE and EMBASE databases are shown in Appendix 2 of the original guideline document. This search has been adapted for the other database. In addition, abstracts from the American Society of Hematology (ASH) (2006 to 2012) and the American Society of Clinical Oncology (ASCO) (2006 to 2013) were searched. Working Group members' files and the reference lists of included articles were searched. The database Clinicaltrials.gov (<http://clinicaltrials.gov/ct2/home>) was searched for ongoing trials. This report contains studies that were included in previous versions and studies resulting from the newly updated search, therefore, the number of the studies in the evidence tables may appear larger than the number of studies retrieved by the update search.

Study Selection Criteria and Protocol

The update review includes a search specific to Burkitt lymphoma and human immunodeficiency virus (HIV)-associated lymphoma, which was not included in the previous version. Articles were selected for inclusion in this systematic review of the evidence if they were fully published reports or published abstracts in the English language comparing rituximab alone with non-rituximab regimens or comparing rituximab combination therapy with non-rituximab regimens and they were:

Lymphoma

1. Randomized controlled trials (RCTs), systematic reviews, meta-analyses, or evidence-based practice guidelines
2. Studies that included adult patients with lymphoma of any type, at any stage, and any histology
3. Studies evaluating one or more of the following outcomes: overall survival (OS), disease control (progression-free survival [PFS], event-free survival [EFS], time to treatment failure [TTF], or response duration [RD]), response rate, quality of life (QOL), or toxicity

Burkitt Lymphoma and HIV-associated Lymphoma

1. Studies that included adult patients with HIV-associated lymphoma or Burkitt lymphoma (both HIV and not HIV)
2. RCTs, systematic reviews, meta-analyses, or evidence-based practice guidelines
3. Other study designs: quasi randomized controlled trials, non-randomized controlled trials, controlled before-and-after studies, prospective cohort studies, retrospective cohort studies, historically controlled trials, nested case-control studies, case-control studies, and before-and-after comparisons (i.e., phase II single arm studies).

Chronic Lymphocytic Leukemia (CLL)

1. RCTs, systematic reviews, meta-analyses, or evidence-based clinical practice guidelines
2. Studies that included patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). For studies including patients with various histological subtypes of lymphoproliferative disorders, outcomes of patients with CLL must be identified separately.
3. Studies evaluating at least one of the following outcomes were reported: OS, disease control (PFS, TTF, EFS, or RD), or toxicity. If response rate is reported, at least one of the above outcomes must also be reported to be included.

Exclusion Criteria

Practice guidelines and systematic reviews older than two years, narrative reviews, letters, comments, editorials, cross sectional studies, case reports/case series and the following publications were excluded:

1. Studies where the population is comprised of: cell lines, animals, patients with other conditions (e.g., Castleman disease), and children
2. No outcomes of interest (i.e., no results for OS, PFS, EFS, TTF, or response duration, response rate, QOL, or toxicity)
3. No comparison to a non-rituximab regimen
4. Population <10 patients
5. Abstract of a systematic review

The following were not considered:

1. Reports evaluating solely patients undergoing stem cell transplantation
2. Abstracts that were reports of interim analyses, as well as abstracts of non-comparative studies (as per Program in Evidence-based Care [PEBC] policy), and systematic reviews that were more than two years old were also not included.

The methodologist screened the titles and the abstracts of the citations identified by the electronic databases and the titles of the abstracts from ASCO and ASH conference proceedings and excluded the citations that reported on studies that did not investigate the use of rituximab or that did not meet the inclusion criteria for design (i.e., were not randomized trials or were not systematic reviews for the target populations or were retrospective studies for lymphoma). The methodologist retrieved the full text of the selected articles in the library and reviewed them.

Number of Source Documents

A total of 344 full text publications were retrieved and screened. One hundred and thirty publications were included representing 56 studies and 5 systematic reviews. See the flow chart in Appendix 4 in the original guideline document for more information on the literature selection process.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data Extraction and Assessment of Study Quality and Potential for Bias

The methodologist extracted data and created evidence tables. Ratios, including hazard ratios (HRs), were expressed with a ratio <1.0 indicating that patients receiving rituximab had a higher probability of survival. All extracted data and information were audited by an independent auditor.

Important quality features, such as required sample size and actual sample, loss to follow-up, blinding, randomization method, allocation concealment, early termination, intention-to-treat analysis, and ethical approval, for each study were extracted.

Synthesizing the Evidence

When clinically homogenous results from two or more trials were available, a meta-analysis was conducted using the Review Manager software (RevMan 5.2) provided by the Cochrane Collaboration. For time-to-event outcomes, HRs, rather than the number of events at a certain time point, were the preferred statistic for meta-analysis, and would be used as reported. If the HR and/or its standard error were not reported, they were derived from other information reported in the study, if possible, using the methods described by Parmar et al. For all outcomes, the generic inverse variance model with random effects, or other appropriate random effects models in RevMan 5.2 was used.

Statistical heterogeneity would be calculated using the χ^2 test for heterogeneity and the I^2 percentage. A probability level for the χ^2 statistic $\leq 10\%$ ($p \leq 0.10$) and/or an $I^2 > 50\%$ would be considered indicative of statistical heterogeneity.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Formation of Working Group

The Hematology Disease Site Group (DSG) asked the Program in Evidence-based Care (PEBC) to develop a guideline on the use of rituximab for lymphoma and chronic lymphocytic leukemia (CLL). In consultation with the Hematology DSG, a Working Group was identified from the DSG membership. This Working Group consisted of five medical oncologists and one methodologist. The Hematology DSG would take responsibility for providing feedback on the guideline as it was being developed and acted as Expert Panel for the document at Internal Review, reviewing the document and requiring changes as necessary before approving it.

Objectives and Research Questions

This Working Group developed the following objective for this guideline in consultation with the Hematology DSG:

- Provide an updated guideline on the use of rituximab in patients with lymphoma and CLL

From this objective, the following research questions were derived to direct the search for available evidence to inform recommendations.

Lymphoma

1. In patients with lymphoma of any type or stage, is rituximab used alone or in combination with chemotherapy more effective than nonrituximab-containing regimens for improving overall survival rates (OS), disease control (as assessed by measures such as progression-free survival rates [PFS], event-free survival rates [EFS], time-to-treatment failure [TTF], or response duration), response rate, or quality of life (QOL)?
2. What is the toxicity associated with the use of rituximab used alone or in combination with chemotherapy compared with nonrituximab-containing regimens?
3. Which patients with lymphoma are more or less likely to benefit from treatment with rituximab compared with those treated with nonrituximab-containing regimens?

Chronic Lymphocytic Leukemia (CLL)

1. What beneficial outcomes are associated with the use of rituximab for the treatment of patients with CLL? Outcomes of interest are OS, disease control (as assessed by measures such as PFS, EFS, TTF, or response duration), and response rate.
2. What is the toxicity associated with the use of rituximab?
3. Which patients are more or less likely to benefit from treatment with rituximab?

Methods

This evidence review is composed of three parts: the evidentiary base of Version 2, the results of the updated search executed in March 2012 and the content of a further update executed in October 2013. The guideline report history is summarized in Appendix 1 of the original guideline document. Each of the searches was developed using a planned two-stage method. This document reports the methods used for the most recent update, methods for previous versions are very similar and are available from PEBC upon request.

1. Search and evaluation of existing systematic reviews: If one or more existing systematic reviews were identified that addressed the research questions and were of reasonable quality, then those systematic reviews would form the core of the evidence review.
2. Systematic review of the primary literature: This review would focus on those areas not covered by existing reviews if any are located and accepted.

Initial Recommendations

Using the evidence review in Section 3 of the original guideline document, the Working Group developed a set of initial recommendations. These initial recommendations were developed through a consideration of the aggregate evidence quality, the potential for bias in the evidence, and the likely benefits and harms of rituximab in patients with lymphoma and CLL. The members of the Working Group considered the values they used in weighing benefits compared with harms, and then made a considered judgement. This process is described in detail for each topic area described in Section 4 of the original guideline document.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Internal Review

Almost all Program in Evidence-based Care (PEBC) documents undergo internal review. This review is conducted by the Expert Panel and the Report Approval Panel (RAP). The Working Group was responsible for incorporating the feedback and required changes of both of these panels, and both panels had to approve the document before it could be sent to External Review.

Expert Panel Review and Approval

The Hematology Disease Side Group (DSG) acted as the Expert Panel for this document. The members of this group were required to submit conflict-of-interest declarations prior to reviewing the document. These declarations are described in Appendix 7 of the original guideline document. The document was approved by formal vote. To be approved, 75% of the Hematology DSG membership must cast a vote or abstain, and of those that vote 75% must approve the document. On November 6, 2014 the Hematology DSG reviewed the document and 80% of the DSG membership cast a vote (20 of 25), either face-to-face or by email. All the voters approved the document as is.

Report Approval Panel Review and Approval

The purpose of the RAP review is to ensure the methodological rigour and quality of PEBC documents. The RAP consists of nine clinicians with broad experience in clinical research and guideline development, and the Director of the PEBC. For each document, three RAP members review the document; the Director and two others. RAP members must not have had any involvement in the development of the guideline prior to Internal Review. All three RAP members must approve the document, although they may do so conditionally. If there is a conditional approval, the Working Group is responsible for ensuring the necessary changes are made, with the Assistant Director of Quality and Methods, PEBC, making a final determination that the RAP's concerns have been addressed.

In December 2014 the RAP reviewed this document. The RAP approved the document, and made a few suggestions for improvement.

External Review by Ontario Clinicians and Other Experts

The PEBC external review process is two-pronged and includes a targeted peer review that is intended to obtain direct feedback on the draft report from a small number of specified content experts, and a professional consultation that is intended to facilitate dissemination of the final guidance report to Ontario practitioners.

Following approval of the document at Internal Review, the Hematology DSG circulated the draft document with recommendations modified as noted under Internal Review, above, to external review participants for review and feedback.

Methods

Targeted Peer Review

During the guideline development process, five targeted peer reviewers from Ontario who are considered clinical and/or methodological experts on the topic were identified by the Working Group and the Hematology DSG. Several weeks prior to completion of the draft report, the nominees were contacted by email and asked to serve as reviewers. Three reviewers agreed and the draft report and a questionnaire were sent via email for

their review. The questionnaire consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and asking whether the draft recommendations should be approved as a guideline. Written comments were invited. The questionnaire and draft document were sent out on January 14, 2015. Follow-up reminders were sent at two weeks (email) and at four weeks (telephone call). The Hematology DSG reviewed the results of the survey.

Professional Consultation

Feedback was obtained through a brief online survey of healthcare professionals who are the intended users of the guideline. All medical oncologists and hematologists in the PEBC database were contacted by email to inform them of the survey. One hundred and fifteen individuals were from Ontario and one from New Brunswick. Participants were asked to rate the overall quality of the guideline and whether they would use and/or recommend it. Written comments were invited. Participants were contacted by email and directed to the survey Web site where they were provided with access to the survey, the guideline recommendations, and the evidence review. The notification email was sent on January 14, 2015. The consultation period ended on February 25, 2015. The Hematology DSG reviewed the results of the survey.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are supported by randomized controlled trials, nonrandomized controlled trials, systematic reviews, and meta-analyses.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

See the "Justification for Recommendation" sections in Section 2 in the original guideline document for benefits in specific patient populations.

Potential Harms

- None of the included studies reported any significant between-group difference in adverse events, except for the RICOVER-60 study in which patients allocated to the 8xR-CHOP-14 arm experienced significantly more anemia and mucositis when compared to patients in the 6xCHOP-14 arm.
- The E4494/C9793 study reported a statistically significantly higher granulocytopenia in the rituximab group (12% versus 4%, $p=0.008$). The CORAL study reported more adverse events in the rituximab group than in the control group during the first 100 days of maintenance (47% versus 42%) with 43 serious adverse events (SAE) in the rituximab group versus 22 SAE in the observation group. Nonhematological toxicity was similar in both groups.
- Three studies reported a significantly greater grade 3-4 lymphopenia in patients treated with rituximab. One study reported a higher rate of infections and neutropenia, and one study reported a higher rate of thrombocytopenia in the rituximab arm compared with chemotherapy alone. Among the non-hematological adverse events, one study reported a statistically significant difference in cardiac toxicity in patients treated with rituximab, while non-significant differences were shown in two studies. Non-significant differences were reported by two studies for neurological toxicities, and for nausea and vomiting in three studies.
- The German Low Grade Lymphoma Study Group (GLSG) study reported a statistically significantly greater grade ≥ 3 lymphopenia in patients treated with rituximab. None of the other studies reported any other significant grade ≥ 3 adverse events.
- The EORTC 20981 study reported a statistically significant higher grade ≥ 3 infections and febrile neutropenia in the rituximab maintenance group than in the observation group; a statistically significant difference in grade 2 to 4 infections has been reported by the PRIMA study. The other studies did not report any statistically significant between-group difference. Infusion-related reactions are described by the most part as mild to moderate, or they are not reported.
- Prolonged rituximab therapy may be associated with hypogammaglobulinemia.

See Tables 2AE, 4AE, 5AE, 6AE, 7AE, 8AE, and 9AE in the original guideline document for more information on grade ≥ 3 adverse events in randomized controlled trials.

Qualifying Statements

Qualifying Statements

Care has been taken in the preparation of the information contained in this report. Nonetheless, any person seeking to apply or consult the report is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or guarantees of any kind whatsoever regarding the report content or use or application and disclaims any responsibility for its application or use in any way.

See the original guideline document for qualifying statements related to each recommendation.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Prica A, Baldassarre F, Hicks LK, Imrie K, Kouroukis TC, Cheung M. Rituximab in lymphoma and chronic lymphocytic leukemia: a clinical practice guideline, version 3. Toronto (ON): Cancer Care Ontario (CCO); 2015 Mar 31. 173 p. (Evidence-based series; no. 6-8). [236 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2005 Feb 17 (revised 2015 Mar 31)

Guideline Developer(s)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

Source(s) of Funding

The Program in Evidence-based Care (PEBC) is a provincial initiative of Cancer Care Ontario (CCO) supported by the Ontario Ministry of Health and Long-Term Care. All work produced by the PEBC is editorially independent from the Ontario Ministry of Health and Long-Term Care.

Guideline Committee

Rituximab in Lymphoma and Chronic Lymphocytic Leukemia Working Group

Composition of Group That Authored the Guideline

Working Group Members: Dr. Anca Prica, Ms. Fulvia Baldassarre, Dr. Tom Kouroukis, Dr. Lisa Hicks, Dr. Kevin Imrie, Dr. Matthew Cheung, the Hematology Disease Site Group*

*See Appendix 7B in the original guideline document for a full list of members.

Financial Disclosures/Conflicts of Interest

In accordance with the Program in Evidence-based Care (PEBC) Conflict of Interest Policy, the guideline authors, the Hematology Disease Site Group (DSG) Panel members, and internal and external reviewers were asked to disclose potential conflicts of interest. Declarations of conflict of interest are reported in Appendices 7A and 7B of the original guideline document.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Imrie K, Stevens A, Meyer R, Hematology Disease Site Group. Rituximab in lymphoma and chronic lymphocytic leukemia: a clinical practice guideline. Toronto (ON): Cancer Care Ontario (CCO); 2005 Dec 22. 46 p. (Evidence-based series; no. 6-8). [65 references]

The EVIDENCE-BASED SERIES report, initially the full original guideline, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the [Cancer Care Ontario Web site](#) for details on any new evidence that has emerged and implications to the guidelines.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the [Cancer Care Ontario \(CCO\) Web site](#) .

Availability of Companion Documents

The following are available:

- Rituxinab in lymphoma and chronic lymphocytic leukemia: a clinical practice guideline, version 3. Summary. Toronto (ON): Cancer Care Ontario (CCO); 2015 Mar 31. 4 p. Electronic copies: Available from the [Cancer Care Ontario \(CCO\) Web site](#) .
- Program in Evidence-based Care handbook. Toronto (ON): Cancer Care Ontario (CCO); 2012. 14 p. Electronic copies: Available from the [CCO Web site](#) .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on August 11, 2005. The information was verified by the guideline developer on September 16, 2005. This summary was updated by ECRI on August 18, 2006. The updated information was verified by the guideline developer on August 23, 2006. This summary was updated by ECRI on January 12, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Rituxan (Rituximab). This summary was updated by ECRI Institute on October 8, 2008 following the U.S. Food and Drug Administration advisory on Rituxan (rituximab). This summary was updated by ECRI Institute on June 29, 2015.

Copyright Statement

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions. Please refer to the [Copyright and Disclaimer Statements](#) posted at the Cancer Care Ontario Web site.

Disclaimer

NGC Disclaimer

The National Guideline Clearinghouse^{â„¢} (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at <http://www.guideline.gov/about/inclusion-criteria.aspx>.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.